## REMARKS

***Status of the Claims***

Claims 2 and new claims 43 – 63 are pending, with claim 2 being independent. Claims 1 and 3 - 42 have been canceled as directed to non-elected subject matter without prejudice to or disclaimer of the subject matter contained therein. Applicants note that they have no intention of abandoning any non-elected subject matter and expressly reserve the right to file one or more continuation and/or divisional applications directed to the non-elected subject matter.

Without conceding the propriety of the rejections, claim 2 has been amended to even more clearly recite and distinctly claim the present invention. New claims 43 – 63 have been added. Support for the amendment to claim 2 and the new claims may be found throughout the specification, including, for example, at page 5, line 7 – page 7, line 2; page 47, line 23 – page 49, line 29; page 70, line 17 – page 74, line 12; page 54, line 1 – page 55, line 2; page 56, line 1 – page 58, line 5; page 58, line 6 – page 60, line 3; and page 60, line 4 – page 61, line 14. Therefore, no new matter has been added.

Applicants respectfully request the Examiner to reconsider and withdraw the outstanding rejections in view of the foregoing amendments and the following remarks.

***Claim Rejections under 35 U.S. C. § 101***

The Examiner has rejected the claimed invention as lacking patentable utility asserting that there is nothing in the claims to indicate that the compounds have been isolated. Applicants respectfully traverse this rejection.

Without conceding the propriety of the rejection, claim 2 has been amended and claims 43 – 63 have been added. Applicants respectfully submit that the presently claimed compounds clearly meet the requirements of 35 U.S.C. 101.

35 U.S.C. 101 requires that some specific, substantial, and credible use be set forth for the invention. Applicants respectfully submit that presently claimed compounds use the enterohepatic circulation of an animal to provide sustained release of orally delivered drugs, thereby providing prolonged therapeutic or prophylactic systemic blood concentrations of the drugs. In the presently claimed

compounds, an orally delivered drug (D) is conjugated to a moiety (T) through a cleavable linker (Y) to provide a compound that is translocated across the intestinal wall of an animal and can participate in the enterohepatic circulation of the animal. Such conjugation allows these compounds, when orally delivered to an animal, to traverse the intestinal wall and to cycle within the enterohepatic circulation of that animal.

The cleavable linker is selected relative to the activity, specificity and localization of enzymatic activity within tissues that comprise the enterohepatic circulation such that a portion of the linker is cleaved and delivered to the systemic blood circulation of the animal during each cycle through the enterohepatic circulation.

In the present application, Applicants have provided examples illustrating how the synthesis of drug/linker/transporter conjugates could be conducted in order to prepare the presently claimed compounds. These syntheses are also illustrated in FIGs. 10-17. Applicants have also provided the key transporter proteins mediating bile acid circulation that can be conjugated with the drug/linker to achieve the disclosed enterohepatic circulation in mammals of the drug to provide sustained release of the orally delivered drugs, thereby providing prolonged therapeutic or prophylactic systemic blood concentrations of the drugs. Applicants have further provided a strategy for achieving enterohepatic recycling of a prodrug or other compound by exploiting intestinal absorption by the peptide transporter, PEPT1, coupled with hepatic uptake and biliary secretion by anion transporters from the OATP and ABC transporter families respectively (e.g. specifically OATP1 and/or OATP2 in the sinusoidal membrane and MRP2 in the canalicular membrane of the hepatocyte).

Accordingly, Applicants respectfully submit that the presently claimed compounds evidence a specific, substantial and credible utility, and thus, the presently claimed compounds meet the requirement of 35 U.S.C. 101. Therefore, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. 101.

***Claim Rejections under 35 U.S.C. § 112, first paragraph***

Claim 2 is rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner contends that the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully submit that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.'" *In re Gosteli,* 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (citations omitted).

In the present application, Applicants have provided examples illustrating how the synthesis of drug/linker/transporter conjugates could be conducted in order to prepare the presently claimed compounds. These syntheses are also illustrated in FIGs. 10-17. Applicants have also provided the key transporter proteins mediating bile acid circulation that can be conjugated with the drug/linker to achieve the disclosed enterohepatic circulation in mammals of the drug to provide sustained release of the orally delivered drugs, thereby providing prolonged therapeutic or prophylactic systemic blood concentrations of the drugs. Applicants have further provided a strategy for achieving enterohepatic recycling of a prodrug or other compound by exploiting intestinal absorption by the peptide transporter, PEPT1, coupled with hepatic uptake and biliary secretion by anion transporters from the OATP and ABC transporter families respectively (e.g. specifically OATP1 and/or OATP2 in the sinusoidal membrane and MRP2 in the canalicular membrane of the hepatocyte).

Accordingly, Applicants respectfully submit that the presently claimed compounds are described in such a way to reasonably convey to one of skill in the art that the Applicants were in possession of the presently claimed compounds at the time the application was filed. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

***Claim Rejections under 35 U.S.C. § 112, second paragraph***

Claim 2 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite. Without conceding the propriety of the rejections, claim 2 has been amended, as provided above, to even more clearly recite and distinctly claim particularly preferred embodiments of Applicant's invention. Applicants note that claim 2 has been amended to more clearly recite and distinctly claim the elements of the compound represented by D-Y-T. With regard to the term "animal," the specification provides that "[a]s used herein, the term "animal" refers to various species such as mammalian and avian species including, by way of example, humans, cattle, sheep, horses, dogs, cats, turkeys, chicken, and the like. Preferably, the animal is a mammal and even more preferably is a human." (page 8, lines 26-29).

Applicants respectfully submit that the present claims particularly point out and distinctly claim the compounds, thus meeting the requirements of 35 U.S.C. §112, second paragraph. Therefore, Applicants respectfully request the withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

***Conclusion***

Without conceding the propriety of the rejections, claim 2 has been amended, as provided above, to even more clearly recite and distinctly claim particularly preferred embodiments of Applicant's invention and to pursue an early allowance. For the reasons noted above, the art of record does not disclose or suggest the inventive concept of the present invention as defined by the claims.

In view of the foregoing remarks, reconsideration of the claims and allowance of the subject application is earnestly solicited. The Examiner is invited to contact the undersigned at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted,

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